

## Complete Summary

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### GUIDELINE TITLE

Stable coronary artery disease.

### BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Stable coronary artery disease. Bloomington (NM): Institute for Clinical Systems Improvement (ICSI); 2006 Apr. 45 p. [70 references]

### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Stable coronary artery disease. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2005 Apr. 49 p.

## COMPLETE SUMMARY CONTENT

SCOPE  
 METHODOLOGY - including Rating Scheme and Cost Analysis  
 RECOMMENDATIONS  
 EVIDENCE SUPPORTING THE RECOMMENDATIONS  
 BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS  
 CONTRAINDICATIONS  
 QUALIFYING STATEMENTS  
 IMPLEMENTATION OF THE GUIDELINE  
 INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT  
 CATEGORIES  
 IDENTIFYING INFORMATION AND AVAILABILITY  
 DISCLAIMER

## SCOPE

### DISEASE/CONDITION(S)

Stable coronary artery disease with or without angina

### GUIDELINE CATEGORY

Evaluation  
 Management  
 Risk Assessment  
 Treatment

## CLINICAL SPECIALTY

Cardiology  
Family Practice  
Internal Medicine

## INTENDED USERS

Advanced Practice Nurses  
Allied Health Personnel  
Health Care Providers  
Health Plans  
Hospitals  
Managed Care Organizations  
Nurses  
Physician Assistants  
Physicians

## GUIDELINE OBJECTIVE(S)

- To improve selection and education of patients with stable coronary artery disease (CAD) on the use of aspirin and antianginal drugs
- To improve patient understanding of management of stable CAD
- To increase the percentage of patients with stable CAD who receive an intervention for modifiable risk factors
- To improve assessment of patient's anginal symptoms
- To increase the use of angiotensin-converting enzyme (ACE) inhibitors in all patients with CAD who also have diabetes and/or left ventricular systolic dysfunction (LVSD), or other cardiovascular diseases

## TARGET POPULATION

Adults aged 18 and over with coronary artery disease with or without angina. Examples include patients with prior myocardial infarctions, prior revascularization (i.e., percutaneous transluminal coronary angioplasty [PTCA], coronary artery bypass graft [CABG]), angiographically proven coronary atherosclerosis, or reliable noninvasive evidence of myocardial ischemia

Patients presenting with angina must meet the following criteria:

- Symptom complex has remained stable for at least 60 days
- No significant change in frequency, duration, precipitating causes, or ease of relief of angina for at least 60 days
- No evidence of recent myocardial damage

## INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation/Risk Assessment

1. History, physical examination and assessment of risk factors

2. Initial laboratory studies (electrocardiogram, fasting lipid profile [total cholesterol, high-density lipoprotein (HDL)-cholesterol, low-density lipoprotein (LDL)-cholesterol, and triglycerides]. Further studies, based on history and physical, may include chest x-ray, measurement of hemoglobin, and tests for diabetes, thyroid function, and renal function, and lipoprotein (a) and highly sensitive c-reactive protein in select patients
3. Evaluation of pattern of angina
4. Exercise electrocardiography (Masters 2-step exercise test, graded exercise test, bicycle test, ergometry)
5. Non-invasive imaging study (myocardial perfusion scintigraphy, stress echocardiography)

#### Treatment/Management

1. Interventions (education, counseling, goal setting, and follow-up) related to reducing modifiable risk factors
2. Pharmacologic therapy (aspirin, clopidogrel, sublingual nitrates, beta-blockers, calcium channel blockers, angiotensin converting enzyme [ACE] inhibitors, combination therapy, statins, and adding clopidogrel to aspirin therapy in patients at increased risk)
3. Nutritional supplement therapy (omega-3 fatty acids)
4. Cardiology consult and/or referral for cardiac catheterization and revascularization procedures [percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass graft (CABG)]

#### MAJOR OUTCOMES CONSIDERED

- Pain control
- Morbidity and mortality associated with coronary artery disease
- Safety of pharmacologic agents

### METHODOLOGY

#### METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

#### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

#### NUMBER OF SOURCE DOCUMENTS

Not stated

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

## RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Key conclusions (as determined by the work group) are supported by a conclusion grading worksheet that summarizes the important studies pertaining to the conclusion. Individual studies are classed according to the system presented below, and are designated as positive, negative, or neutral to reflect the study quality.

### Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

### Study Quality Designations

The quality of the primary research reports and systematic reviews are designated in the following ways on the conclusion grading worksheets:

Positive: indicates that the report or review has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis.

Negative: indicates that these issues (inclusion/exclusion, bias, generalizability, and data collection and analysis) have not been adequately addressed.

Neutral: indicates that the report or review is neither exceptionally strong or exceptionally weak.

Not Applicable: indicates that the report is not a primary reference or a systematic review and therefore the quality has not been assessed.

#### Classes of Research Reports:

##### A. Primary Reports of New Data Collection:

###### Class A:

- Randomized, controlled trial

###### Class B:

- Cohort study

###### Class C:

- Non-randomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

###### Class D:

- Cross-sectional study
- Case series
- Case report

##### B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

###### Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

###### Class R:

- Consensus statement
- Consensus report
- Narrative review

###### Class X:

- Medical opinion

#### METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses  
Systematic Review with Evidence Tables

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

Published cost analyses were reviewed.

## METHOD OF GUIDELINE VALIDATION

Clinical Validation-Pilot Testing  
Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Institute Partners: System-Wide Review

The guideline draft, discussion, and measurement specification documents undergo thorough review. Written comments are solicited from clinical, measurement, and management experts from within the member medical groups during an eight-week period of "Critical Review."

Each of the Institute's participating medical groups determines its own process for distributing the guideline and obtaining feedback. Clinicians are asked to suggest modifications based on their understanding of the clinical literature coupled with their clinical expertise. Representatives from all departments involved in implementation and measurement review the guideline to determine its operational impact. Measurement specifications for selected measures are developed by the Institute for Clinical Systems Improvement (ICSI) in collaboration with participating medical groups following general implementation of the guideline. The specifications suggest approaches to operationalizing the measure.

Guideline Work Group: Second Draft

Following the completion of the "Critical Review" period, the guideline work group meets 1 to 2 times to review the input received. The original guideline is revised as necessary and a written response is prepared to address each of the suggestions received from medical groups. Two members of the Cardiovascular Steering Committee carefully review the Critical Review input, the work group responses, and the revised draft of the guideline. They report to the entire committee their assessment of two questions: (1) Have the concerns of the medical groups been adequately addressed? (2) Are the medical groups willing

and able to implement the guideline? The committee then either approves the guideline for pilot testing as submitted or negotiates changes with the work group representative present at the meeting.

#### Pilot Test

Medical groups introduce the guideline at pilot sites, providing training to the clinical staff and incorporating it into the organization's scheduling, computer, and other practice systems. Evaluation and assessment occurs throughout the pilot test phase, which usually lasts for three months. Comments and suggestions are solicited in the same manner as used during the "Critical Review" phase.

The guideline work group meets to review the pilot sites' experiences and makes the necessary revisions to the guideline; the Cardiovascular Steering Committee reviews the revised guideline and approves it for implementation.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC) and the Institute for Clinical Systems Improvement (ICSI): In addition to updating their clinical guidance, ICSI has developed a new format for all guidelines. Key additions and changes include: combination of the annotation and discussion section; the addition of "Key Points" at the beginning of most annotations; the inclusion of references supporting the recommendations; and a complete list of references in the Supporting Evidence section of the guideline. For a description of what has changed since the previous version of this guidance, refer to "[Summary of Changes -- April - 2006](#)."

The recommendations for stable coronary artery disease are presented in the form of two algorithms, accompanied by detailed annotations. The algorithm for [Stable Coronary Artery Disease](#) has 20 components and addresses the evaluation and overall management of the patient with the disease. The second algorithm, with 11 components, addresses [Pharmacologic Therapy](#). Clinical highlights and selected annotations (numbered to correspond with the algorithms) follow.

Class of evidence (A-D, M, R, X) and conclusion grade (I-III, Not Assignable) definitions are repeated at the end of the "Major Recommendations" field.

#### Clinical Highlights

- Prescribe aspirin in patients with stable coronary artery disease if there are no medical contraindications. (Annotation #21a)
- Evaluate and treat the modifiable risk factors, which include smoking, sedentary activity level, stress, hyperlipidemia, obesity, hypertension, and diabetes. (Annotation #5)
- Patients with chronic stable coronary artery disease should be on statin therapy regardless of their lipid levels unless contraindicated. (Annotation #5)

- Perform prognostic testing in patients whose risk determination remains unclear. This may precede or follow an initial course of pharmacologic therapy. (Annotations #7, 8, 9, 10)
- Refer the patient for cardiovascular consultation when clinical assessment indicates the patient is at high risk for adverse events, the non-invasive imaging study or electrocardiogram (EKG) indicates the patient is at high risk for an adverse event, or medical treatment is ineffective. (Annotations #11, 16)
- For relief of angina, prescribe beta-blockers as first line medication. If beta-blockers are contraindicated, nitrates are the preferred alternative. Calcium channel blockers may be an alternative medication if the patient is unable to take beta-blockers or nitrates. (Annotation #21e)

### Stable Coronary Artery Disease Algorithm Annotations

#### 1. Patients with Stable Coronary Artery Disease (CAD)

This guideline applies to patients with coronary artery disease either with or without angina. Examples include patients with prior myocardial infarctions, prior revascularization (i.e., percutaneous transluminal coronary angioplasty [PTCA], coronary artery bypass graft [CABG]), angiographically proven coronary atherosclerosis, or reliable noninvasive evidence of myocardial ischemia.

A patient presenting with angina must meet the following criteria:

- Symptom complex has remained stable for at least 60 days
- No significant change in frequency, duration, precipitating causes, or ease of relief of angina for at least 60 days
- No evidence of recent myocardial damage

The patient may already have undergone some diagnostic workup as a result of a prior presentation of chest pressure, heaviness, and/or pain with or without radiation of the pain and/or shortness of breath. Initial care of such patients falls under the auspices of the National Guideline Clearinghouse (NGC) summary of the Institute for Clinical Systems Improvement (ICSI) [Diagnosis and Treatment of Chest Pain and Acute Coronary Syndrome \(ACS\)](#) guideline.

Evidence supporting this recommendation is of class: R

#### 2. Perform Appropriate History Taking, Physical Examination, Laboratory Studies, and Patient Education

Thorough history taking and physical examination including medication and compliance reviews are important to confirm diagnosis, to assist in risk stratification, and to develop a treatment plan. Important points to elicit on history taking are:

- Recognize women may have atypical symptoms of cardiac ischemia. These may include fatigue, shortness of breath (SOB) without chest



pain, nausea and vomiting, back pain, jaw pain, dizziness, and weakness

- History of previous heart disease
- Possible nonatheromatous causes of angina pectoris (e.g., aortic stenosis)
- Comorbid conditions affecting progression of CAD
- Symptoms of systemic atherosclerosis (i.e., claudication, transient ischemic attacks [TIAs], and bruits)
- Severity and pattern of symptoms of angina pectoris

The physical examination should include a thorough cardiovascular examination as well as evaluation for evidence of hyperlipidemia, hypertension, peripheral vascular disease, congestive heart failure, anemia, thyroid disease, and renal disease.

Initial laboratory studies should include an electrocardiogram and a fasting lipid profile (total cholesterol, high-density lipoprotein [HDL] cholesterol, calculated low-density lipoprotein [LDL] cholesterol, and triglycerides). Further tests, based on history and physical examination findings, may include chest x-ray, measurement of hemoglobin, and tests for diabetes, thyroid function, and renal function.

An important aspect to treatment of stable coronary artery disease is education to help the patient understand the disease processes, prognosis, treatment options, and signs of worsening cardiac ischemia so that prompt medical assistance is sought when necessary and appropriate. Education may be accomplished in a number of ways among the various medical groups. It may be ongoing, occur in a formal class, and/or be done at the provider visit. Instruction on the proper use of aspirin (ASA) and sublingual nitroglycerin, as needed, should also be reviewed at this time.

Evidence supporting this recommendation is of class: R

## 5. Address Modifiable Risk Factors and Comorbid Affectors

Comorbid conditions that affect myocardial ischemia may include hypertension, anemia, thyroid disease, hypoxemia, and others.

Modifiable risk factors for coronary heart disease need to be evaluated and may include smoking, inadequate physical activity, stress, hyperlipidemia, obesity, hypertension, and diabetes mellitus. Intervention involving any risk factor pertinent to the patient is encouraged, and may include education, goal setting, and follow-up as necessary.

See Appendix A, "Comorbid Conditions" in the original guideline document for treatment recommendations in the presence of comorbid conditions.

Evidence supporting this recommendation is of class: R

Emerging Risk Factors

An association between homocysteine levels and cardiovascular disease has been demonstrated. The recently published NORVIT trial and HOPE 2 trial found that folate and vitamins B6 and B12 did not reduce the risk of recurrent cardiovascular events in patients with vascular disease. These supplements cannot be recommended as routine treatment in patients with Stable CAD.

In select patients, clinicians may want to consider obtaining a lipoprotein (a), and highly sensitive C-reactive protein (hsCRP). Highly sensitive CRP and related markers of inflammation may provide useful prognostic information and help guide further therapy for patients with CAD.

## Smoking

Refer to the NGC summary of the ICSI guideline [Tobacco Use Prevention and Cessation for Adults and Mature Adolescents](#) for recommendations regarding smoking cessation.

## Sedentary Activity Level

An important aspect of the provider's role is to counsel patients regarding appropriate work, leisure activities, eating habits, and vacation plans. Patients should be encouraged to exercise regularly to obtain cardiovascular benefit and to enhance their quality of life. The American College of Cardiology endorses a minimum schedule of 30 to 60 minutes of aerobic activity (walking, jogging, etc.) three to four times per week, supplemented by an increase in daily lifestyle activities (walking breaks at work, gardening, etc.) Medically supervised programs are recommended for moderate- to high-risk patients. Exercise can be an important adjunct to modification of risk factors such as hypertension, hyperlipidemia, and obesity. In addition, it can enhance patients' perception of their quality of life. Strenuous activities should be modified if they produce severe or prolonged angina; caution is needed to avoid consistent reproduction of ischemic symptoms or situations that may precipitate ischemic complications. Education is critical in achieving these goals.

Evidence supporting this recommendation is of class: A

## Stress

Psychophysiologic stress is a notable feature of the relationship between myocardial ischemia and the patient's daily environment. Depressive symptoms are common in stable CAD patients, with prevalence estimates ranging from 15 to 30%. Depression should be screened for and appropriately treated.

## Hyperlipidemia

A fasting lipid profile should be evaluated for appropriate patients with stable coronary artery disease. Secondary prevention is important in these patients who should be treated aggressively for hyperlipidemia. Many patients will

require both pharmacologic and non-pharmacologic interventions to reach target goals.

Target goals for hyperlipidemic patients with coronary artery disease include:

- LDL - less than 100 mg/dL
- HDL - 40 mg/dL or greater
- Triglycerides - less than 150 mg/dL

There is now an ideal LDL-cholesterol (LDL-C) goal of less than 70 mg/dL for patients considered to be very high risk. Several trials have shown clinical benefit using high dose statins to treat to lower LDL levels.

At present the clinician will need to individualize therapy with statins by the degree of risk in their patients, considering a target LDL of 70 or less, especially for patients at highest risks. Very high risk patients include patients with established cardiovascular disease plus any of the following: 1) multiple major risk factors, such as diabetes; 2) severe or poorly-controlled risk factors, especially smoking; 3) metabolic syndrome associated risk factors (triglycerides greater than 200 mg/dL, HDL less than 40 mg/dL); and 4) patients with acute coronary syndromes. The benefits in reducing cardiac events with high dose statin therapy will need to be weighed against the higher potential for side effects, and the potential for increased non-cardiac mortality as seen in the TNT trial, which is either real, or due to chance. Further trials comparing different treatment intensities of statins should bring more clarity regarding which patients benefit most with the least side effects.

Refer to the NGC summary of the ICSI guideline [Lipid Management in Adults](#) for recommendations on cholesterol lowering.

Every effort should be made to ensure all patients with coronary artery disease receive optimal lipid therapy. Statin medications are strongly supported as first-line medications due to compelling evidence of mortality reduction from multiple clinical trials.

If patients are intolerant to a statin, clinicians are strongly encouraged to have the patient try other statins in reduced doses before ruling out all statins.

The PROSPER trial showed a significant risk reduction in myocardial infarction (MI) in the elderly, therefore age alone should not preclude treatment. The Heart Protection Study also showed benefit in patients up to age 80.

Patients with chronic stable coronary artery disease should be on statin therapy regardless of their lipid levels unless contraindicated. [Conclusion Grade I: See Conclusion Grading Worksheet A -- Annotation #5 (Statin Therapy) in the original guideline document]

Evidence supporting this recommendation is of classes: A, R

Obesity

The American Heart Association (AHA) now considers obesity to be a major risk factor for CAD, particularly if the body mass index (BMI) is greater than 30. The loss of as little as 10 to 15% of an individual's weight can impact and decrease mortality.

Evidence supporting this recommendation is of class: X

### Hypertension

General health measures include the treatment of hypertension, which is not only a risk factor for development and progression of atherosclerosis but also causes cardiac hypertrophy, augments myocardial oxygen requirements, and thereby intensifies myocardial ischemia in patients with obstructive coronary disease.

Refer to the NGC summary of the ICSI guideline [Hypertension Diagnosis and Treatment](#) for recommendations regarding blood pressure management. The recommended target blood pressure is 130/180 or less.

### Diabetes

Patients with diabetes should have aggressive lipid and blood pressure management (similar to patients with coronary artery disease), and should be treated per the recommendations of the ICSI [Lipid Management in Adults](#) and [Hypertension Diagnosis and Treatment](#) guidelines.

Refer to the NGC summary of the ICSI guideline [Management of Type 2 Diabetes Mellitus](#) for recommendations regarding management of diabetes.

Every attempt should be made to achieve meticulous glucose control in patients with diabetes, as there is a clear relationship between lower hemoglobin A1c's and lower risk of myocardial infarction.

Evidence supporting this recommendation is of classes: A, B

### Hormone Replacement Therapy (HRT)

Risk-benefit analyses unequivocally support NOT starting HRT for primary prevention. Should a patient already on HRT present with acute coronary syndrome or be at risk for venous thromboembolism (i.e., prolonged immobilization), HRT should be discontinued immediately. Clinical judgment is required in making the decision whether to continue HRT in other circumstances. Refer to the NGC summary of the ICSI guideline [Menopause and Hormone Therapy](#) for more information.

Evidence supporting this recommendation is of class: A

## 6. Assessment Yields High Risk of Adverse Event?

Some patients are considered to be at high risk for infarction or death on the basis of history, physical examination, and initial laboratory findings. Patients

presenting with accelerating symptoms of angina (New York Heart Association [NYHA] Class III or IV, see the original guideline document, Appendix C, "Grading Angina Pectoris"), symptoms of peripheral vascular disease, or symptoms of left ventricular dysfunction should be referred to a cardiologist unless precluded by other medical conditions.

#### 7. Need for Prognostic Testing?

Prognostic testing is appropriate for patients in whom risk determination remains unclear after the initial evaluations have been completed, or in whom cardiac catheterization is deemed inappropriate by the cardiologist. Prognostic testing may precede or follow an initial course of pharmacologic therapy.

Evidence supporting this recommendation is of class: R

#### 8. Patient/EKG Allows Exercise Electrocardiography?

Sensitivity of exercise electrocardiography (Masters 2-Step Exercise Test, Graded Exercise Test, Bicycle Test, Ergometry), may be reduced for patients unable to reach the level of exercise required for near maximal effort, such as:

- Patients taking beta-blockers
- Patients in whom fatigue, dyspnea, or claudication symptoms develop
- Patients with vascular, orthopedic, or neurological conditions who cannot perform leg exercises

Reduced specificity may be seen in patients with abnormalities on baseline EKG, such as those taking digitalis medications, and in patients with left ventricular hypertrophy or left bundle branch block. See the NGC summary of the ICSI [Cardiac Stress Test Supplement](#) for more information.

Evidence supporting this recommendation is of class: R

#### 10. Perform Non-Invasive Imaging Study

A non-invasive imaging study such as myocardial perfusion scintigraphy or stress echocardiography should best meet the patient's needs while providing the most clinical usefulness and cost-effectiveness within the provider's institution. An imaging study should be selected through discussion with the cardiologist or imaging expert.

Evidence supporting this recommendation is of class: R

#### 11. Results Yield High Risk of Adverse Event?

Exercise electrocardiography and prognostic imaging studies may yield results that indicate high, intermediate or indeterminate, or low risk of adverse clinical events. High-risk patients should have a cardiology consultation unless they are not considered to be potential candidates for revascularization. Patients who are at intermediate or indeterminate risk may benefit from

cardiology consultation or further noninvasive imaging if an exercise electrocardiogram has been performed, or both. Low-risk patients can generally be managed medically, with a good prognosis. Low-risk patients may benefit from angiography if the diagnosis remains unclear; however, angiography is unlikely to alter outcome in these patients.

Evidence supporting this recommendation is of class: R

#### 14. Follow Regularly to Assess Risk Factors, Profile, Responses to Treatment

There is no consensus in the literature regarding frequency of follow-up; ongoing management needs and follow-up should be individualized.

Patient perception of symptoms may impact the effect of the symptoms on quality of life and medical management.

Refer to Appendix C, "Grading of Angina Pectoris" in the original guideline document for information on grading angina pectoris.

Evidence supporting this recommendation is of class: D

#### 15. Worsening in Angina Pattern?

A new occurrence of angina or a worsening in the chronic stable angina pattern is to be considered to be present when any of the following occur: the symptom complex becomes less stable; there is a change in frequency, duration, precipitating causes, or ease in relief of angina; or there is evidence of recent myocardial damage.

#### 16. Change Suggests Need for Cardiology Referral?

When such change is no longer managed by alterations in the pharmacologic therapy prescribed, cardiology consultation or referral for possible invasive intervention may be appropriate.

See Appendix C, "Grading Angina Pectoris," in the original guideline document for information on grading angina pectoris.

Evidence supporting this recommendation is of class: R

### [Pharmacologic Therapy Algorithm Annotations](#)

#### 21a. Patient Education and Review Principles of Medication Therapy: ASA, $\pm$ Clopidogrel, Sublingual Nitroglycerin, Statins

The use of one aspirin tablet daily (81 to 162 mg) is strongly recommended unless there are medical contraindications.

Recent studies on antiplatelet therapy have shown that ASA dose in the range of 75 to 150 mg should be given for the long term prevention of serious vascular events in high risk patients, and that there may be a reduced benefit when increasing the dose over 150 mg daily. Doses available to most clinicians are in increments of 81 mg; therefore the recommended dose range is 81 to 162 mg daily.

It remains difficult to conclude whether enteric-coated (EC)-ASA is gastro-protective or not, but clinicians should not assume that it is any safer than regular or buffered aspirin, and should treat it with the same level of caution.

Patients for whom aspirin is contraindicated (examples are provided in the NGC Complete Guideline Summary field labeled "Contraindications"), or insufficient, should be treated with clopidogrel (Plavix®) 75 mg daily indefinitely, in view of greater safety, equivalent efficacy, and cost savings when compared with ticlopidine as an antiplatelet treatment.

In appropriately selected patients, an aspirin dose of 81 mg is recommended for patients who are on chronic clopidogrel therapy. Different doses of aspirin may apply in the setting of acute coronary syndrome; refer to the NGC summary of the ICSI guideline [Diagnosis and Treatment of Chest Pain and Acute Coronary Syndrome](#) for aspirin dosing.

Aspirin and/or clopidogrel should be prescribed to all patients with stable coronary disease [Conclusion Grade I: See Conclusion Grading Worksheet B - Annotation #21a (ASA/Clopidogrel) in the original guideline document.]

In patients with mild, stable CAD, drug therapy may be limited to short-acting sublingual nitrates on an as-needed basis. Use of lower dose (i.e., 0.3 mg or one-half of a 0.4-mg tablet) may reduce the incidence of side effects such as headache or hypotension in susceptible patients.

For more information regarding drug selection, see Appendix B, "Medication Tables," in the original guideline document.

Evidence supporting the aspirin recommendation is of classes: A, C, D, M, R

#### 21b. Nutritional Supplement Therapy

The American Heart Association recommends inclusion of omega-3 fatty acids in patients with stable CAD because of evidence from randomized controlled trials.

The recommended daily amount of omega-3 fatty acids in patients with stable coronary artery disease is 1 gram of eicosapentaenoic acid/docosahexaenoic acid (EPA/DHA) by capsule supplement, the equivalent amount in alpha-linolenic acid (ALA) from vegetable source, or by eating daily fatty fish. The amounts of omega-3 fatty acids in various foods are found in Appendix D in the original guideline document. Plant-based sources of omega-3 fatty acids would be ground flax seed, flax seed oil, walnut oil, canola oil, and soybean oil. Daily fish meals can be difficult for patients to maintain, and there are issues of potential environmental

contaminants including mercury, polychlorinated biphenyls (PCBs), dioxin, and others. Because of this, capsule supplements may be preferred although there is no uniformity of EPA/DHA content or purity. Patients should consult their health providers or nutritionists regarding this issue.

Dietary and non-dietary intake of n-3 polyunsaturated fatty acids may reduce overall mortality, mortality due to myocardial infarction, and sudden death in patients with stable CAD. [Conclusion Grade II: See Conclusion Grading Worksheet C - Annotation #21b (Omega III) in the original guideline document]

High doses of vitamin E supplement (greater than 400 IU/day) may increase or cause mortality and should be avoided.

Evidence supporting this recommendation is of classes: A, M, R

#### 21c. Use of Angiotensin Converting Enzyme (ACE) Inhibitors for Risk Reduction

Among patients with stable angina, ACE inhibitors are most beneficial to patients with left ventricular dysfunction post myocardial infarction, persistent hypertension, and diabetes.

Evidence supporting this recommendation is of class: A

#### 21d. Does Patient Need Daily Antianginal Therapy?

The decision to initiate daily drug therapy for CAD is based upon the symptom complex of the patient in combination with findings from the history, physical examination, laboratory studies, and prognostic testing.

Evidence supporting this recommendation is of classes: A, R

#### 21e. Prescribe Monotherapy

##### Beta-Blocking Agents

Beta-blockers should be used in all status post-myocardial infarction patients, based on studies showing mortality reduction. They are also the preferred first-line therapy for reducing symptoms of angina in patients with stable coronary artery disease. Drugs with intrinsic sympathomimetic activity should be avoided. Abrupt withdrawal of all beta-blockers should be avoided.

##### Long-Acting Nitrates

If beta-blockers cannot be prescribed as first-line therapy, nitrates are the preferred alternative first-line therapy because of efficacy, low cost, and relatively few side effects. Tolerance to long-acting nitrates is an important clinical issue in some patients and can be avoided by appropriate daily nitrate-free intervals.

##### Adverse Interactions between Nitrates and Phosphodiesterase-5 Inhibitors



Patients with stable CAD should be advised that due to potentially life-threatening hypotension, phosphodiesterase-5 inhibitors (like sildenafil [Viagra®], vardenafil [Levitra®], and tadalafil [Cialis®]) are absolutely contraindicated if they have used nitrates within the last 24 hours.

In any patient evaluated for acute coronary insufficiency, nitrates must also be avoided if there is a history of sildenafil or phosphodiesterase-5 inhibitor use in the previous 24 to 48 hours (avoid nitrates for 24 hours after Viagra® and Levitra®; avoid nitrates for 48 hours after Cialis®). All other interventions, including all non-nitrate antianginal medications may be used for these patients.

### Calcium Channel Blocker

For patients who are unable to take beta-blockers or long-acting nitrates, the use of calcium channel blockers has been shown to be clinically effective in decreasing symptoms of angina. Calcium channel blockers have not been proven to reduce mortality. Because beta-blockers have reduced mortality in the post myocardial infarction period, they are the preferred agent for patients with stable coronary artery disease. Dihydropyridines as monotherapy may exacerbate angina.

Evidence supporting this conclusion is of class: A, R

### 21g. Prescribe Combination Therapy

Combination therapy may be necessary in selected patients, but it increases side effects and cost. A combination of beta-blockers and long-acting nitrates is preferred because of cost, efficacy, and reduced potential for adverse side effects. The following factors should be considered when beta-blockers and calcium channel blockers are combined:

- This combination may not be better than either agent used alone in maximum tolerated doses.
- If angina persists at the maximum optimal dose of beta-blocker, then addition of a calcium channel blocker is likely to reduce angina and improve exercise performance.
- Addition of verapamil or diltiazem to a beta-blocker does not usually enhance therapy, and may precipitate symptomatic bradycardia, but addition of a beta-blocker to nifedipine can have enhanced effects.
- With left ventricular dysfunction, sinus bradycardia, or conduction disturbances, treatment with calcium channel blockers and beta-blockers should be avoided or initiated with caution. In patients with conduction system disease, the preferred combination is nifedipine and a beta-blocker.
- The combination of dihydropyridines and long-acting oral nitrates is usually not optimal because both are potent vasodilators.
- If side effects prohibit increased doses but symptoms persist, selected patients may need low doses of multiple drug therapy.

Evidence supporting this recommendation is of classes: A, R

### 21h. Combination Therapy Effective?

If after several attempts at adjusting the medications a therapeutic combination is not achieved for the patient, a cardiology consultation or referral may be appropriate.

#### Definitions:

##### Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

##### Classes of Research Reports:

###### A. Primary Reports of New Data Collection:

###### Class A:

- Randomized, controlled trial

###### Class B:

- Cohort study

###### Class C:

- Non-randomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test

- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

## CLINICAL ALGORITHM(S)

Detailed and annotated clinical algorithms are provided in the original guideline document for:

- [Stable Coronary Artery Disease](#)
- [Pharmacologic Therapy](#)

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

In addition, key conclusions contained in the Work Group's algorithm are supported by a grading worksheet that summarizes the important studies pertaining to the conclusion. The type and quality of the evidence supporting these key recommendations is graded for each study.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- An effective management plan for stable coronary artery disease (CAD) may result in pain control, reduced morbidity and mortality associated with CAD, and safe and cost-effective use of pharmacologic agents.
- Application of this guideline may optimize medical therapy through improved selection and education of patients with stable CAD on the use of aspirin and anti-anginal drugs; improve patient understanding of management of stable CAD; increase the percentage of patients with stable CAD who receive an intervention for modifiable risk factors; improve assessment of patient's anginal symptoms; and increase the use of angiotensin-converting enzyme (ACE) inhibitors in all patient with CAD who also have diabetes and/or left ventricular systolic dysfunction, or other cardiovascular diseases.

## POTENTIAL HARMS

- Thrombotic thrombocytopenic purpura (TTP) may occur with clopidogrel, but it appears to be 1/100th as frequent as thrombotic thrombocytopenic purpura from ticlopidine.
- Addition of verapamil or diltiazem to a beta-blocker may precipitate symptomatic bradycardia.
- In patients with left ventricular dysfunction, sinus bradycardia, or conduction disturbances, treatment with calcium channel blockers and beta-blockers should be avoided or initiated with caution.
- Tolerance to long-acting nitrates is an important clinical issue in some patients and can be avoided by appropriate daily nitrate-free intervals

## CONTRAINDICATIONS

### CONTRAINDICATIONS

#### Adverse Interactions between Nitrates and Phosphodiesterase-5 Inhibitors

Patients with stable coronary artery disease should be advised that due to potentially life-threatening hypotension, phosphodiesterase 5 inhibitors (sildenafil [Viagra®], vardenafil [Levitra®], and tadalafil [Cialis®]) are absolutely contraindicated if they have used nitrates within the last 24 hours.

In any patient evaluated for acute coronary insufficiency, nitrates must also be avoided if there is a history of sildenafil or phosphodiesterase-5 inhibitor use in the previous 24 to 48 hours (avoid nitrates for 24 hours after Viagra® and Levitra®; avoid nitrates for 48 hours after Cialis®).

#### Aspirin

Examples of precautions/contraindications to aspirin are:

- Patients allergic to aspirin
- Patients with gastrointestinal disorders
  - Recent gastrointestinal bleeding and active treatment for peptic ulcer disease are contraindications
- Patients with recent intracranial bleeding

- Intracranial bleeding within the past six weeks is a contraindication.
- Any history of intracranial bleeding necessitates evaluation on a case-by-case basis.
- Patients with bleeding disorders or those receiving other anticoagulants
- Patients with uncontrolled hypertension
  - Systolic blood pressure is greater than 180 mmHg; diastolic blood pressure is greater than 110 mmHg
- Patients regularly taking non-steroidal anti-inflammatory drugs (NSAIDs)
  - Combined use of aspirin and NSAIDs may increase risk of bleeding. Enteric-coated aspirin with careful monitoring for clinical signs of gastropathy may be an acceptable strategy for patients regularly taking NSAIDs. Caution should be used in prescribing COX-2 inhibitors to patients with coronary artery disease, as there is evidence of a class effect on cardiovascular risks.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.
- This clinical guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients are urged to consult a health care professional regarding their own situation and any specific medical questions they may have.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for general implementation, a medical group can choose to concentrate on the implementation of that guideline. When four or more groups choose the same guideline to implement and they wish to collaborate with others, they may form an action group.

In the action group, each medical group sets specific goals they plan to achieve in improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment, and tobacco cessation.

Detailed measurement strategies are presented in the original guideline document to help close the gap between clinical practice and the guideline

recommendations. Summaries of the measures are provided in the National Quality Measures Clearinghouse (NQMC).

## IMPLEMENTATION TOOLS

Clinical Algorithm  
Patient Resources  
Pocket Guide/Reference Cards  
Quality Measures

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## RELATED NQMC MEASURES

- [Stable coronary artery disease \(CAD\): percentage of patients with stable CAD who have aspirin use documented in the medical record.](#)
- [Stable coronary artery disease \(CAD\): percentage of patients with stable CAD who have had a lipid profile determination at target \(less than 100\) and measured within the last year.](#)

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Stable coronary artery disease. Bloomington (NM): Institute for Clinical Systems Improvement (ICSI); 2006 Apr. 45 p. [70 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

1994 Jul (revised 2006 Apr)

### GUIDELINE DEVELOPER(S)

## Institute for Clinical Systems Improvement - Private Nonprofit Organization

### GUIDELINE DEVELOPER COMMENT

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers, Allina Medical Clinic, Altru Health System, Aspen Medical Group, Avera Health, CentraCare, Columbia Park Medical Group, Community-University Health Care Center, Dakota Clinic, ENT Specialty Care, Fairview Health Services, Family HealthServices Minnesota, Family Practice Medical Center, Gateway Family Health Clinic, Gillette Children's Specialty Healthcare, Grand Itasca Clinic and Hospital, HealthEast Care System, HealthPartners Central Minnesota Clinics, HealthPartners Medical Group and Clinics, Hutchinson Area Health Care, Hutchinson Medical Center, Lakeview Clinic, Mayo Clinic, Mercy Hospital and Health Care Center, MeritCare, Mille Lacs Health System, Minnesota Gastroenterology, Montevideo Clinic, North Clinic, North Memorial Care System, North Suburban Family Physicians, Northwest Family Physicians, Olmsted Medical Center, Park Nicollet Health Services, Pilot City Health Center, Quello Clinic, Ridgeview Medical Center, River Falls Medical Clinic, Saint Mary's/Duluth Clinic Health System, St. Paul Heart Clinic, Sioux Valley Hospitals and Health System, Southside Community Health Services, Stillwater Medical Group, SuperiorHealth Medical Group, University of Minnesota Physicians, Winona Clinic, Ltd., Winona Health

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### GUIDELINE COMMITTEE

Cardiovascular Steering Committee

### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Work Group Members: Greg Lehman, MD (Work Group Leader) (Park Nicollet Clinic) (Internal Medicine); Greg Barsness, MD (Mayo Clinic) (Cardiology); Dale Duthoy, MD (Family HealthServices Minnesota) (Family Medicine); Jim Haefemeyer, MD (HealthPartners Medical Group) (Family Medicine); Fritz Arnason, MD (Park Nicollet Clinic) (General Internist); Phil Kofron, MD, MPH (Park Nicollet Clinic) (General Internist); Susan M. Hanson, RD (Park Nicollet Institute) (Health Education); Shauna Schad, RN, CNS (Mayo Clinic) (Nursing); Peter Marshall, PharmD (HealthPartners Medical Group) (Pharmacy); Raed D. Abughazaleh (University of Minnesota) (Pharmacy Student); Amy Murphy, MHHA (Institute for Clinical Systems Improvement) (Measurement Advisor); Brent Metfessel, MD

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## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

In the interest of full disclosure, the Institute for Clinical Systems Improvement (ICSI) has adopted a policy of revealing relationships work group members have with companies that sell products or services that are relevant to this guideline topic. The reader should not assume that these financial interests will have an adverse impact on the content of the guideline. Readers of the guideline may assume that only work group members listed below have potential conflict of interest to disclose.

Phillip M. Kofron, MD has received honoraria and expense reimbursement from Kos and Pfizer for speaker training. He has a speaker consulting agreement with Pfizer but he has not made presentations or received speaker fees from Kos or Pfizer to date.

No other work group members have potential conflicts of interest to disclose.

ICSI's conflict of interest policy and procedures are available for review on ICSI's website at [www.icsi.org](http://www.icsi.org).

## GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Stable coronary artery disease. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2005 Apr. 49 p.

## GUIDELINE AVAILABILITY

Electronic copies: Available from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](http://www.icsi.org).

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: [www.icsi.org](http://www.icsi.org); e-mail: [icsi.info@icsi.org](mailto:icsi.info@icsi.org).

## AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Stable coronary artery disease. Executive summary. Bloomington (MN): Institute for Clinical Systems Improvement, 2006 Apr. 1 p. Electronic copies: Available from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](http://www.icsi.org).
- ICSI pocket guidelines. May 2005 edition. Bloomington (MN): Institute for Clinical Systems Improvement, 2005. 362 p.



Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: [www.icsi.org](http://www.icsi.org); e-mail: [icsi.info@icsi.org](mailto:icsi.info@icsi.org).

## PATIENT RESOURCES

The following is available:

- Stable coronary artery disease. Bloomington (MN): Institute for Clinical Systems Improvement, 2006 May. 18 p.

Electronic copies: Available from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](http://www.icsi.org).

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

## NGC STATUS

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